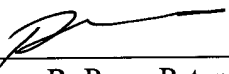


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Doran R. Pace, Patent Attorney

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AMENDMENT UNDER 37 CFR §1.111
Examining Group 1655
Patent Application
Docket No. GJE-35
Serial No. 09/463,549

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner : Arun Chakrabarti, Ph.D.
Art Unit : 1655
Applicant : Daniel Henry Densham
Serial No. : 09/463,549
Filed : January 27, 2000
Conf. No. : 6468
For : Nucleic Acid Sequence Analysis

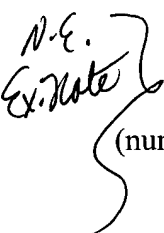
Assistant Commissioner for Patents
Washington, D.C. 20231

AMENDMENT UNDER 37 CFR §1.111

Sir:

In response to the Office Action dated August 20, 2001, please amend the above-identified patent application as follows:

In the Specification


Please replace original figures 1-3 (numbered as pages 1/5 through 5/5) with new figures 1-3 (numbered as pages 1/5 through 5/5) attached hereto.

In the Claims

Please cancel claims 2, 22-29 and 35, without prejudice.

Please substitute the following claims:

Claim 1 (amended):

1. A method for sequencing a polynucleotide, comprising the steps of:
- (i) reacting a target polynucleotide with a polymerase enzyme immobilised on a solid support, and complementary nucleotides, under conditions sufficient for the polymerase reaction; and
 - (ii) detecting an effect consequent on the incorporation of a specific nucleotide complementary to the target polynucleotide, to thereby determine the sequence of the target polynucleotide, the detection being carried out by measuring radiation.

Claim 3 (amended):

3. The method according to claim 1, wherein steps (i) and (ii) are conducted with each of the complementary nucleotides in turn, until incorporation is detected, and then repeated.

Claim 4 (amended):

4. The method according to claim 1, wherein step (i) is conducted with all the complementary nucleotides present.

Claim 5 (amended):

5. The method according to claim 1, wherein the complementary nucleotides comprise a 3' blocking group which is removed after the polymerase reaction.

Claim 6 (amended):

6. The method according to claim 5, wherein the blocking group is selectively removed by pulsed monochromatic light.

Claim 7 (amended):

7. The method according to claim 5, wherein the complementary nucleotides comprise a further blocking group at the terminal phosphate group of the triphosphate chain, and the further blocking group is removed prior to the removal of the 3' blocking group.

B2 ✓
Claim 8 (twice amended):

8. The method according to claim 7, wherein the further blocking group is selectively removed by pulsed monochromatic light under conditions different from those required to remove the 3' blocking group.

B3
Claim 20 (amended):

20. The method according to claim 19, wherein the incorporation of the complementary nucleotide is detected using NMR.

Claim 30 (amended):

30. The method according to claim 1, wherein steps (i) and (ii) are conducted with each of the complementary nucleotides in turn, until incorporation is detected, and then repeated.

B4
Claim 31 (amended):

31. The method according to claim 1, wherein step (i) is conducted with all the complementary nucleotides present.

Claim 32 (amended):

32. The method according to claim 6, wherein the complementary nucleotides comprise a further blocking group at the terminal phosphate group of the triphosphate chain, and the further blocking group is removed prior to the removal of the 3' blocking group.

Remarks

Claims 1-35 are pending in the subject application. By this Amendment, Applicant has canceled claims 2, 22-29, and 35 and amended claims 1, 3-8, 20, and 30-32. Support for the amendments can be found in the claims as filed and throughout the subject specification, including at page 4, lines 1-2. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 1, 3-21 and 30-34 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

In the Office Action, the Examiner indicates that claims 22-29 have been canceled. Applicant notes that while claims 22-29 and 35 were not elected in Applicant's Response to the Restriction Requirement dated July 16, 2001, the claims were not canceled at that time. However, those claims are now being canceled by this Amendment.

Applicant has submitted with this Amendment formal Figures 1, 2A, 2B, 2C, and 3 in response to the Notice of Draftsperson's Patent Drawing Review. Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

Claims 1-21 and 30-34 are rejected under 35 USC §112, second paragraph. Applicant asserts that the claims are definite. However, in order to lend greater clarity to the claimed subject matter, Applicant has amended the claims. Specifically, Applicant has amended claim 1 to include a step for determining the sequence of the target polynucleotide in the claimed method. In regard to the rejection of claims 1 and 3 for lack of antecedent basis, Applicant has amended the claims to recite "complementary" nucleotides. In regard to the rejection of claims 6 and 8, Applicant has amended the claims to replace "can be" with "is." Accordingly, reconsideration and withdrawal of the rejection under 35 USC §112, second paragraph, is respectfully requested.

Claims 1-9, 21, and 30-34 are rejected under 35 USC §102(b) as anticipated by Tsien *et al.* (WO 91/06678). The Examiner asserts that the Tsien *et al.* reference teaches Applicant's method for sequencing a polynucleotide. Applicant respectfully traverses and asserts that the Tsien *et al.* reference does not teach or suggest the claimed invention.

As the Examiner is undoubtedly aware, in order to anticipate, a single reference must disclose within the four corners of the document each and every element and limitation contained in the rejected claim. *Scripps Clinic & Research Foundation v. Genentech Inc.*, 18 USPQ2d 1001, 1010

(Fed. Cir. 1991). Applicant respectfully asserts that the Tsien *et al.* reference does not teach or suggest the use of an immobilized polymerase. Although the Examiner asserts that Tsien *et al.* disclose an immobilized polymerase, Applicant respectfully asserts that the Tsien *et al.* reference only teaches that the DNA or its primer is immobilized to a solid support (see, for example, page 32, lines 9-36, through to page 34, line 34, of the Tsien *et al.* reference). Since the Tsien *et al.* reference does not teach the immobilized polymerase element, it cannot anticipate the claimed invention. Accordingly, reconsideration and withdrawal of the rejection under 35 USC §102(b) is respectfully requested.

Claims 1-9, 15, 17, 18, 21, and 30-34 are rejected under 35 USC §103(a) as obvious over Tsien *et al.* (WO 91/06678) in view of Schwarz *et al.* (1991). In addition, claims 1-10, 21, and 30-34 are rejected under 35 USC §103(a) as obvious over Tsien *et al.* (WO 91/06678) in view of Chang *et al.* (U.S. Patent No. 5,801,042). Also, claims 1-9, 11, 12, 21, and 30-34 are rejected under 35 USC §103(a) as obvious over Tsien *et al.* (WO 91/06678) in view of O'Donnell (U.S. Patent No. 6,221,642). Additionally, claims 1-9, 13, 21, and 30-34 are rejected under 35 USC §103(a) over Tsien *et al.* (WO 91/06678) in view of Rosenthal *et al.* (WO 93/21340). Further, claims 1-9, 14, 21, and 30-34 are rejected under 35 USC §103(a) as obvious over Tsien *et al.* (WO 91/06678) in view of Vind (U.S. Patent No. 6,159,687). Finally, claims 1-9, 16, 19-21, and 30-34 are rejected under 35 USC §103(a) as obvious over Tsien *et al.* (WO 91/06678) in view of Smith *et al.* (U.S. Patent No. 5,753,439). The Tsien *et al.* reference is cited as the primary reference in each of the above rejections. Applicant respectfully traverses each of these grounds of rejections.

In regard to the Examiner's reliance on the primary reference, Tsien *et al.* (WO 91/06678), Applicant hereby incorporates and reasserts his remarks concerning this reference as set forth in response to the rejection under 35 USC §102(b). As noted above, the Tsien *et al.* reference does not teach or suggest the use of an immobilized polymerase.

The secondary references relied upon by the Examiner in the §103 rejection, *i.e.*, Schwarz *et al.* (1991), Chang *et al.* (U.S. Patent No. 5,801,042), O'Donnell (U.S. Patent No. 6,221,642), Rosenthal *et al.* (WO 93/21340), Vind (U.S. Patent No. 6,159,687), and Smith *et al.* (U.S. Patent No. 5,753,439), do not cure the deficiencies of the primary reference. Applicant respectfully asserts that

none of the secondary references, taken alone or in combination, teach or suggest the claimed invention.

The Examiner asserts that the Schwarz *et al.* (1991) reference teaches the detection of nucleic acid incorporation by surface plasmon resonance signal over time in the infra-red spectrum. The Examiner relies upon the Chang *et al.* patent for teaching the competitive inhibitor of the polymerase enzyme. The Examiner relies upon the O'Donnell patent for teaching the beta-2 dimer complex of the *E. coli* DNA polymerase III with the target polynucleotide. The Examiner further asserts that the Rosenthal *et al.* reference teaches the Taq polymerase and that the Vind patent teaches the reverse transcriptase as the polymerase. Finally, the Examiner concludes that the Smith *et al.* patent teaches the detection of nucleotides by NMR using electromagnetic radiation. However, none of the cited references teach or suggest the use of an immobilized polymerase. Thus, neither the primary reference, nor the secondary references, teach or suggest Applicant's claimed invention. Accordingly, reconsideration and withdrawal of the rejections 35 USC §103(a) is respectfully requested.

Applicant would like to bring to the Examiner's attention a Supplemental Information Disclosure Statement listing references for consideration in the prosecution of the subject application which is being submitted in conjunction with the filing of this Amendment. Applicant respectfully requests that the references be considered and made of record by the Examiner in the subject application.

It should be understood that these amendments have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicant's agreement with or acquiescence in the Examiner's position.

In view of the foregoing remarks and amendments to the claims, Applicant believes that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicant invites the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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DRP/sl

Attachments: Marked-Up Version of Amended Claims; new Figures 1, 2A, 2B, 2C, and 3.